Anatomy Physiology & Biochemistry
International Journal
ISSN: 2476-1400

Review Article
Volume 6 Issue 5 - August 2023
DOI: 10.19080/APBIJ.2023.06.555698

Anatomy Physiol Biochem Int J

Every Organism has its own "The Boss". Behavior of Bacteria Compared to Behavior of Eukaryotes

Julius Adler*

Department of Biochemistry and Department of Genetics, University of Wisconsin-Madison, USA

Submission: July 13, 2023; **Published:** August 02, 2023

***Corresponding author:** Julius Adler, Department of Biochemistry and Department of Genetics, University of Wisconsin-Madison, USA

Email id: juliusadler1@gmail.com

Abstract

Every organism has its own "The Boss". The evidence for this is presented here. The research of Helen Barbas on the rhesus monkey has been extended to organisms in general. This is supported by mutants lacking it in the eukaryote Drosophila. Also, bacteria have "The Boss." The location of "The Boss" is different in eukaryotes and in bacteria.

Keywords: Organisms; Eukaryote Drosophila; Bacteria; Chemotaxis in Bacteria; Biology; Metabolism; Genetics; Neurobiology; Psychology; Biochemistry; Neuroscience

Introduction

Is there something that directs each organism? To me one of the most interesting questions of behavior is how an organism makes a decision about what to do when it encounters conflicting stimuli. A study of this leads into the mechanism that is used to control the organism, see (Figure 1) [1]. Modern studies of biology have revealed a universality among living things. For example, all organisms have much in common when it comes to their metabolism and genetics. Is it not possible that all organisms share common mechanisms for responding to stimuli by movement. Just as the higher organism 's machinery for metabolism and genetics appears to have evolved from processes already present in the lowest forms, so it is possible that the nervous system and behavior of higher organisms evolved from chemical reactions that can be found even in the most primitive living things. From this point of view, one may hope that a knowledge of the mechanisms of motility and chemotaxis in bacteria might contribute to our understanding of neurobiology and psychology. But then it was discovered by Linda Buck & Richard Axel [2] that neurobiology employs its own pathway.

First line of evidence about the boss

I have done research on the behavior of bacteria for 40 years (1960 to 2000). This is summarized in my review [3]. Then I started research on non-bacteria (Drosophila fruit flies) and "found" The Boss, page 60 of "My Life with Nature", Annual Review of Biochemistry 2011, see (Figure 1) above: I proposed there that The Boss is the thing that directs behavior of organisms. This was described further in my review [4]. These two introductory articles report the beginning of the idea of The Boss. More recently, Lar Vang and I [5] actually present evidence for the existence of The Boss in Drosophila fruit flies; consider also six related papers by Vang and Adler in bioRxiv.

We proposed in Vang and Adler October 2018 that all organisms have something in charge of them, namely "The Boss", I quote from there: "All things that an organism does are controlled by The Boss...While so far. The Boss has been just an idea, this idea may now be supported by mutants studied here. These motile mutants may fail to respond to sensory stimuli due to lacking the behavioral part of The Boss". It is a novel idea: all the properties of every kind of organism are controlled by a mechanism called "The Boss". The Boss directs both the outside and the inside of each organism. The Boss in some form is to be found in microorganisms, plants, animals, and humans.

How does The Boss lead? The control by The Boss is not always direct: many aspects are delegated to managers, who delegate to foremen, who delegate to workers. So far it is largely the workers that have been studied, and sometimes the foremen are revealed, and rarely the managers, but The Boss has remained largely hidden. The present study is related to the research of Helen Barbas on the orbitofrontal cortex in the brain of the rhesus monkey. Barbas discovered in the rhesus monkey (2000, (Figure 2) below) that the orbitofrontal cortex receives information from the sensory cortices, namely the visual, auditory, somatosensory, gustatory, and olfactory data as it is just received, and in addition it receives information from the amygdala, which contains data about emotion and memory of past events. Then the information from the sensory cortices and the information from the amygdala fuse in the orbitofrontal cortex. Barbas says that "the orbitofrontal cortex is thus capable of sampling the entire external and internal environment and may act as an environmental integrator". And then, she tells, that this brings about a response by the organism.

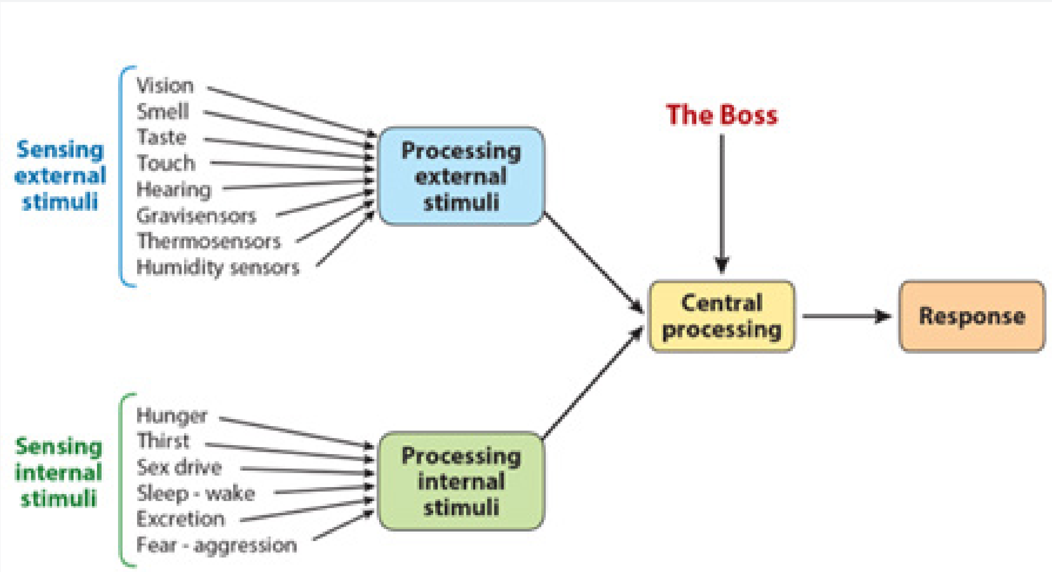

Figure 1: This is Figure 13 of page 60 of "My Life with Nature", Annual Review of Biochemistry [3], which says: "The mechanism of behavior. This applies to all organisms: microorganisms, plants, animals, including humans." Sensory inputs produce Central processing, which is controlled by The Boss.

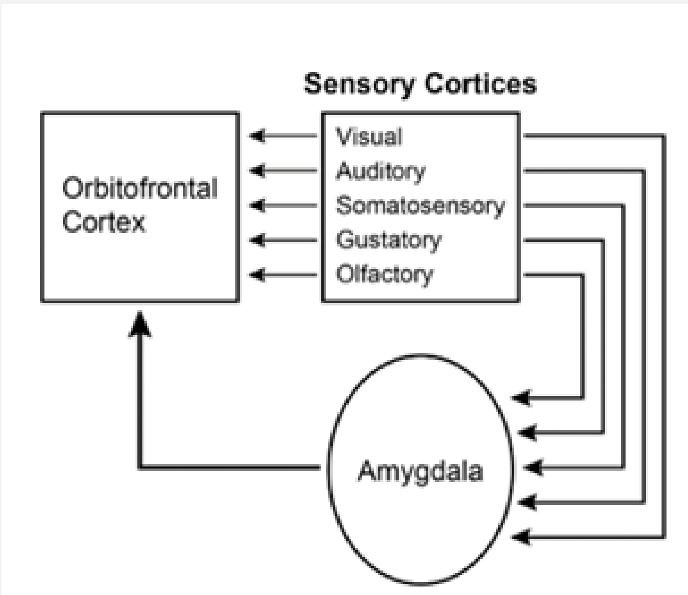

Figure 2: The orbitofrontal cortex in the rhesus monkey according to Barbas, Brain Research Bulletin [38].

How to cite this article: Julius A. Every Organism has its own "The Boss". Behavior of Bacteria Compared to Behavior of Eukaryotes. Anatomy Physiol Biochem Int J: 2023; 6(5): 555698. DOI: 10.19080/APBIJ.2023.06.555698

Her research on this began in Barbas and Mesulman [6]. For a recent (2022) report by Barbas of her work and her thinking see her [7]. That mechanism shown in (Figure 2), together with all that controls it, I call "The Boss". I propose here that every organism has some form of The Boss.

Second line of evidence about the boss

To try to find evidence that might test the existence of The Boss, we looked for mutants missing The Boss in Drosophila fruit flies. These are mutants that are motile but can't decide what to do. They don't respond to outside attractants and repellents or to inside stimuli like hunger, thirst, and sleep. So, all responses are shut off for these motile mutants. Thus, they are defective in the response mechanism, which I regard to be The Boss. A summary of such mutants found is presented next. We isolated motile mutants of Drosophila fruit flies that lack all behavioral responses at an elevated temperature (34°C) presumably by lacking The Boss there, but they do have the responses at room temperature where The Boss still exists (Adler and Vang [8]).

In addition, we isolated motile mutants of fruit flies that lack all behavioral responses at both the elevated temperature and room temperature by presumably lacking The Boss, as reported in Vang and Adler [5]. Then there has to be some alternative way to allow survival. In those mutants the defect is found to be in RNA splicing and RNA helicase by Vang and Adler [5]. How are RNA splicing and RNA helicase involved in the mechanism of The Boss? The answer is not known yet. The Boss is considered to be universal. People, too, would have The Boss, like other primates do. An example might even be found as far away as in trees, see "The Hidden Life of Trees, What They Feel, How They Communicate" by forest scientist Peter Wohlleben, 2016, and see the following photo of trees growing away from the shade of a building, which might be caused by their presumed Boss leading trees away already in their youth (Figure 3).

Figure 3: Trees growing away from low light produced by the shade of a building. Photo by Hilde Wohl Adler, 2023.

See also these related reports Ryan Joseph, Anida Devineni, and Ian Kung [9] studied competing behavioral drives in oviposition in Drosophila (Biological Sciences). [10] Nilay Yapici, Manuel Zimmer, and Ana Domingos studied "Cellular and molecular basis of decision-making" (EMBO reports), in which they presented "Here, we review recent research in mice, Drosophila melanogaster and Caenorhabditis elegans that analyses the molecular and cellular mechanisms underlying decision making." Our knowledge of how DNA, RNA, and proteins are made, and how this is controlled, is now extensive for DNA

How to cite this article: Julius A. Every Organism has its own "The Boss". Behavior of Bacteria Compared to Behavior of Eukaryotes. Anatomy Physiol Biochem Int J: 2023; 6(5): 555698. DOI: 10.19080/APBIJ.2023.06.555698

synthesis ([11], Zakrzewska-Czerwinska et al., 2007; [12,13], for RNA synthesis ([14], Malys and McCarthy, 2010; and Nakagawa et al., 2010), and for protein synthesis [15-19]. As an example, there is a time during the cell cycle when DNA synthesis is turned on and a time when it is turned off. The proposal here is that there is a master control, The Boss, that dictates what shall be the state of synthesis of DNA, RNA, and proteins, see (Figure 4) next.

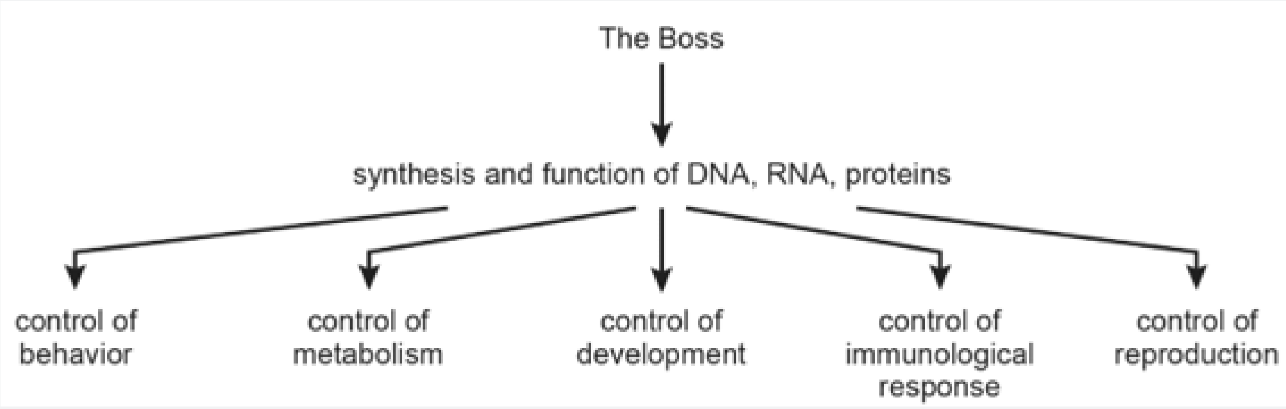

Figure 4: The role of The Boss. From Adler [4].

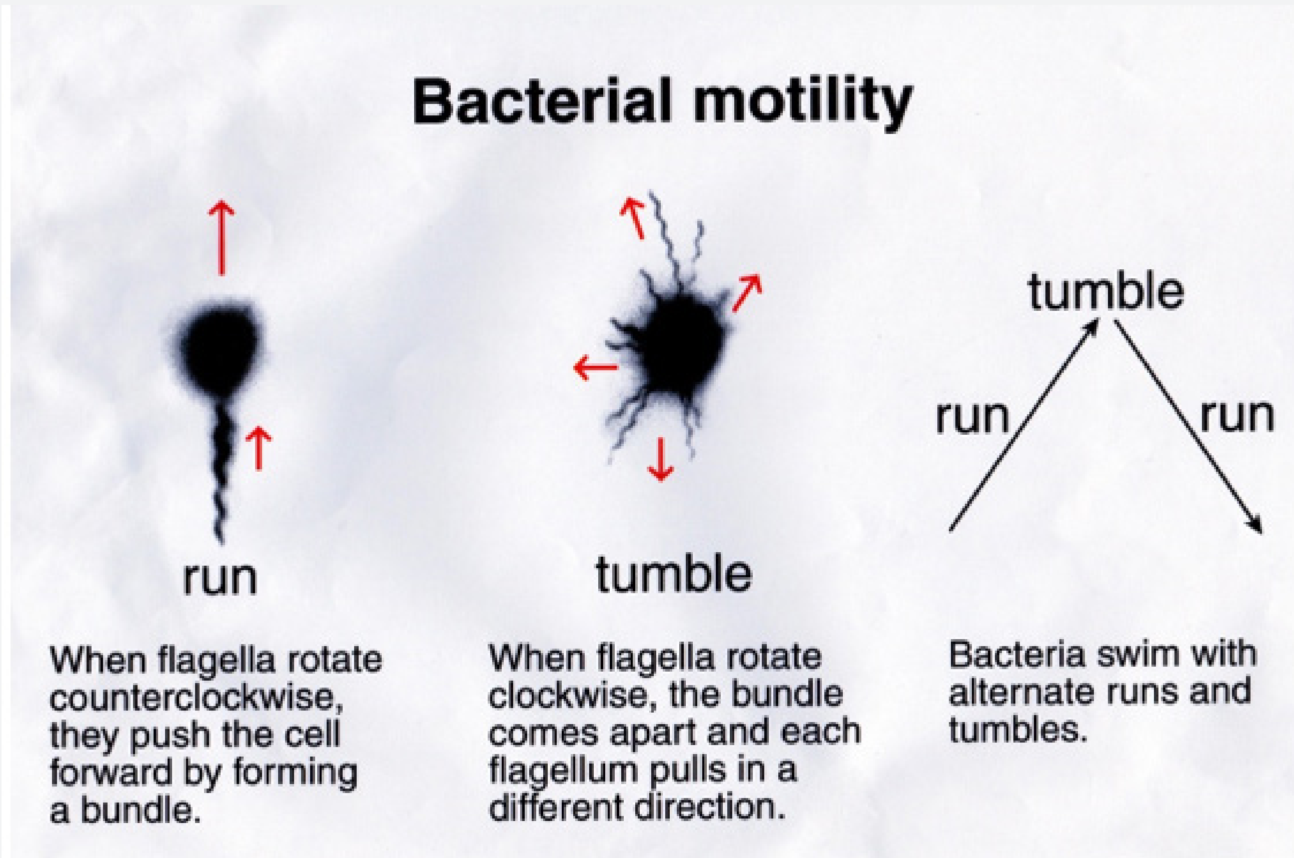

Figure 5: Running and tumbling. This is in accord with older references (Engelmann, Pfeffer, Rothert, Jennings) cited by Adler [1]. It is in accord with Howard Berg & Robert Anderson,[40]; Michael Silverman & Melvin Simon [56]; and Steven Larsen, Robert Reader, Edward Kort, Wung-Wai Tso, & Julius Adler [48].

How to cite this article: Julius A. Every Organism has its own “The Boss”. Behavior of Bacteria Compared to Behavior of Eukaryotes. Anatomy Physiol Biochem Int J: 2023; 6(5): 555698. DOI: 10.19080/APBIJ.2023.06.555698

The Boss is the thing in every organism that controls the organism. The Boss directs the synthesis and activity of DNA, RNA, and proteins, and thereby is in charge of behavior, metabolism, development, immunological response, and reproduction.

Third line of evidence about the boss

Bacteria swim by running and tumbling to see the next figure. Running allows movement toward an attractant, tumbling allows lack of movement to avoid a repellent (Figure 5).

Does The Boss exist in bacteria? I think so. Here I quote Adler & Tso, [20]; "Apparently bacteria have a data-processing system that receives opposing signals from the chemoreceptors for positive and negative chemotaxis, sums these signals, and sends the result to the flagella for action". The data-processing system can now be termed "The Boss", or instead there is a still unknown step ahead of data processing called "The Boss" that directs data-processing.

I'm the one who discovered that bacteria have a part that controls their behavior. This is described in Adler [21]. It is reviewed by Thomas Silhavy, "Chemoreeceptors in bacteria, J. Adler" in Microbiology Centenary Perspective [22]. It is now known as methyl-accepting chemotaxis protein (MCP) in [3] or as chemoreceptor complex. It is located in the "head" of a bacterium: see JR Maddock & Lucy Shapiro [23]; so, The Boss might be expected to be located at the pole (the "head") of a bacterium.

Daniel Koshland Jr has reported [24] "...The bacterial processing system not only can give additive responses to combinations of like stimuli, but it can integrate the effects of several different stimuli in an algebraic manner. Clearly such a property is similar to that of a neuron, which receives excitatory and inhibitory signals and must have the ability to integrate this information...The sensory system of a bacterium is a relatively simple input-output system with a processing capability that is moderately simple. It is in no way as complex as the human brain, and it could be argued that it is appreciably simpler than an individual neuron...A particularly interesting feature of the bacterium is that it encompasses many of the principles of higher behavioral systems within a single cell. It has specialized response systems that ultimately lead into a centralized system."

Coli has a mechanism that overrules all other mechanisms

Zachary Burton, Carol Gross, Kathleen Watanabe, & Richard Burgess [25] and James Lupski, Bob Smiley, & Nigel Godson [26] discovered that *E. coli* has an operon that controls all three of the most basic processes-DNA synthesis, RNA synthesis, and protein synthesis. How is that operon turned on and off? It may well be by The Boss [3].

Fourth line of evidence: Location of the boss

In bacteria and in eukaryotes the goal of the organism is the same, namely to respond to attractants and repellents, but the mechanism of achieving the goal is different. This difference between bacteria and eukaryotes is reported next.

Filamentous bacteria [like *E. coli* today] were first present around 3 billion years ago, according to [27] "The Unicellular Ancestry of Animal Development". Then much later, about 0.6 billion years ago, filamentous protozoa appeared, says King. These were the precursors of Metazoa: beetles, frogs, and animals, according to King. "The transition to multicellularity that launched the evolution of animals from protozoa marks one of the most pivotal, and poorly understood, events in life's history" says King. David Robson tells in [28], "The story of the brain begins in the ancient oceans long before the first animals appeared. The single-celled organisms that swam or crawled in them may not have had brains, but they did have sophisticated ways of sensing and responding to their environment." Andrew Knoll tells in 2003 and [29] that filamentous prokaryotes decorate the fossil record beginning earlier, perhaps 3.2 billion years ago. King has continued and expanded her work, see Rosanna Alegado & King [30], also Thibaut Brunet & King [31].

I now suppose that the behavior of present-day bacteria might be based on origins in filamentous bacteria of about 3 billion years ago, while the behavior of present-day eukaryotes, for example fruit flies, might be based on origins in filamentous Protozoa about 0.6 billion years ago. I would call these "studies based on early behavior" and "studies based on later behavior" respectively, or the "early form" and the "late form".

So, there is a difference in mechanism of sensing by bacteria and by eukaryotes: bacteria sense stimuli by use of 2-trans-membrane methyl-accepting receptors in their single cells in order to produce behavioral change, while eukaryotes sense stimuli by means of 7-trans-membrane receptors in receptor cells which then lead on to the brain which then produces behavioral change.

Summary

Although The Boss occurs in both bacteria and eukaryotes, the place where The Boss comes into play is different in the two. In eukaryotes that place is associated with Central processing, see (Figure 1) above. In bacteria that place is data-processing, see data-processing system above, but another possibility for The Boss in bacteria is a previous step, still unknown, which controls data-processing.

Conclusion

In bacteria, too, each individual organism is led by its own The Boss. As to the chemistry of The Boss, this is unknown. It could be DNA, or it could be RNA that functions independently of DNA. The genes for The Boss would likely be made of DNA; however, since RNA seems to have been present in organisms before there was any DNA, according to ideas of Carl Woese (1968), David

How to cite this article: Julius A. Every Organism has its own "The Boss". Behavior of Bacteria Compared to Behavior of Eukaryotes. Anatomy Physiol Biochem Int J: 2023; 6(5): 555698. DOI: 10.19080/APBIJ.2023.06.555698

Baltimore [32], and Walter Gilbert [33], The Boss may be made of RNA genes present already before DNA in earlier times.

Putting it all together

a) The Boss is the director of behavior. The Boss occurs in eukaryotes and also in bacteria. Each individual organism has its own The Boss.

b) Bacteria (prokaryotes) sense attractants and repellents by use of 2-trans-membrane methyl-accepting receptors while eukaryotes sense them by use of 7-trans-membrane receptors. Bacteria act on them by using internal Che proteins, while eukaryotes act on them by sending the sensed information to the brain. The Che proteins of bacteria tell the flagella how to respond, while the brain tells the muscles how to respond.

c) There are two related forms for behavior of organisms, one used by bacteria, and one used by eukaryotes: these are the "early form" and the "late form". Their ancestry is described [34-65].

Acknowledgement

I thank NIH for forty years of support of this study of behavior of *E. coli*. I am most grateful to The Camille and Henry Dreyfus Foundation for six years of support of the undergraduate research program on behavior of Drosophila. Lar Vang has been an associate research specialist here. I am sorry to report his death, due to pancreatic cancer, I am most sad. Robert Kreber, a research specialist in Barry Ganetzky's laboratory, has helped us greatly in studies of the genetics of our mutants. I thank Barry for teaching me about fruit flies. I am thankful to Laura Vanderploeg for the artwork.

References

1. Adler J (1966) Chemotaxis in bacteria. Science 153(3737): 708-716.
2. Buck L, Axel R (1991) A novel multigene family may encode odorant receptors: A molecular basis for odor recognition. Cell 65(1): 175-187.
3. Adler J (2011) My life with nature. Annual Review of Biochemistry 80: 42-70.
4. Adler J (2016) A search for the Boss: The thing inside each organism that is in charge. Anatomy Physiology & Biochemistry International Journal 1(1): 001-0013.
5. Vang LL, Adler J (2018) Drosophila mutants that are motile but respond poorly to all stimuli tested: Mutants in RNA splicing and RNA helicase, mutants in The Boss. bioRxiv p.1-17.
6. Barbas H, Mesulam MM (1981) Organization of afferent input subdivisions of area 8 in the rhesus monkey. Journal of Comparative Neurology 200(3): 407-431.
7. Barbas H (2022) Frontal Cortex in book Neuroscience in the 21st Century, from Basic to Clinical. In: D. W. Pfaff pp.1707-1753.
8. Adler J, Vang LL (2016) Decision making by Drosophila flies. BioRxiv p.1-31.
9. Joseph RM, Devineni AV, King IFC, Heberlein U (2009) Oviposition preference for and positional avoidance of acetic acid provide a model for competing behavioral drives in Drosophila. Biological Sciences PNAS 106927): 11352-11357.
10. Yapici N, Zimmer M, Domingos AI (2014) Cellular and molecular basis of decision making. EMBO reports 15(10): 1023-1035.
11. Kaguni JM (2006) DnaA: Controlling the Initiation of Bacterial DNA Replication and More. Annual Review of Microbiology 60: 351-371.
12. Katayama T, Ozaki S, Keyamura K and Fujimitsu K (2010) Regulation of the replication cycle: conserved and diverse regulatory systems for DnaA and oriC. Nature Reviews Microbiology 8(3): 163-170.
13. Masai H, Matsumoto S, You Z, Yoshizawa-Sugata N, Oda M (2010) Eukaryotic chromosome DNA replication: where, when, and how?. Annual Review of Biochemistry 79: 89-130.
14. Jackson RJ, Hellen CUT, Pestova TV (2010) The mechanism of eukaryotic translation initiation and principles of its regulation. Nature Reviews Molecular Cell Biology 11(2): 113-127.
15. Thomas MC, Chiang CM (2006) The General transcription machinery and general cofactors. Critical Reviews in Biochemistry and Molecular Biology 41(3): 105-178.
16. Passalacqua KD, Varadarajan A, Ondov BD, Okou DT, Zwick ME, et al. (2009) Structure and complexity of a bacterial transcriptome. Journal of Bacteriology 191(10): 3203-3211.
17. Jiang C, Pugh BF (2009) Nucleosome positioning and gene regulation: advances through genomics. Nature Reviews Genetics 10(3): 161-172.
18. Sorek R, Cossart P (2010) Procaryotic transcriptomics: a new view on regulation, physiology and pathogenicity. Nature Reviews Genetics 11: 9-16.
19. Kim TM, Park PJ (2011) Advances in analysis of transcriptional regulatory networks. Wiley Interdisciplinary Reviews, Systems Biology and Medicine 3(1): 21-35.
20. Tso WW, Adler J (1974) Negative chemotaxis in Escherichia coli. Journal of Bacteriology 118(2): 560-576.
21. Adler J (1993) Chemoreceptors in bacteria. Science.
22. Silhavy TJ (1999) Microbiology: A Centenary Perspective, edited by WK Joklik, LG Ljungdahl, AD O Brien, A von Graevenitz, C Yanofsky, Society for Microbiology Press, Washington DC, pp.428.
23. Maddock JR, Shapiro L (1993) Polar location of the chemoreceptor complex in the Escherichia coli cell. Science 259(5102): 1717-1723.
24. Koshland DE Jr (1980) Bacterial chemotaxis in relation to neurobiology. Annual Review of Neuroscience 3: 43-75.
25. Burton ZF, Gross CA, Watanabe KK and Burgess RR (1983) The operon that encodes the sigma unit of RNA polymerase also encodes ribosomal protein S21 and DNA primase in E. coli K12. Cell 32(2): 335-349.
26. Lupski JR, Smiley BL, and Godson GN (1983) Regulation of the rpsU-dnaG-rpoD macromolecular synthesis operon and the initiation of DNA replication in Escherichia coli K-12. Molecular and General Genetics 189(1): 48-57.
27. King N (2004) The unicellular ancestry of animal development. Developmental Cell 7(3): 313-325.
28. Robson D (2011) A brief history of the brain. New Scientist.
29. Knoll AH (2015) Life on a Young Planet. Princeton University Press In: The First Three Billion Years of Evolution on Earth - Updated Edition pp. 296.
30. Alegado RA, King N (2014) Bacterial influences on animal origins. Cold Spring Harbor Perspectives in Biology 6(11): a016162.

31. Brunet T, King N (2017) The origin of animal multicellularity and cell differentiation. Developmental Cell 43: 124-140.

32. Baltimore D (1980) Evolution of RNA viruses. Annals of the New York Academy of Sciences 354: 492-497.

33. Gilbert W (1986) Origin of Life, the RNA World. Nature 319: 618.

34. Adler J (1969) Chemoreceptors in bacteria. Science 166(3913): 1588-1597.

35. Adler J (1975) Chemotaxis in bacteria. Annual Review of Biochemistry 44: 341-356.

36. Adler J, Tso WW (1974) "Decision"-making in bacteria: chemotactic response of Escherichia coli to conflicting stimuli. Science 184: 1292-1294.

37. Armstrong JB, Adler J, Dahl MM (1967) Nonchemotactic mutants of Escherichia coli. Journal of Bacteriology 93(1): 390-398.

38. Barbas H (2000) Connections underlying the synthesis of cognition, memory, and emotion in primate prefrontal cortices. Brain Research Bulletin 52(5): 319-330.

39. Barbas H (2015) General cortical and special prefrontal connections: Principles from structure to function. Annual Review of Neuroscience 38: 269-289.

40. Berg HC, Anderson RA (1973) Bacteria swim by rotating their flagellar filaments. Nature 245: 380-382.

41. Brembs B (2021) The brain as a dynamically active organ. Biochemical and Biophysical Research Communications 564: 55-69.

42. Carlen M (2017) What constitutes the prefrontal cortex? Science 358: 478-482.

43. Dormazet LT, Tautz D (2008) An evolutionary origin of genes associated with human genetic diseases. Molecular Biology and Evolution 25(12): 2699-2707.

44. Hangarter RP (1997) Gravity, light and plant form. Plant, cell & environment 20(6): 796-800.

45. Hazelbauer GL (2012) Bacterial chemotaxis: The early years of molecular studies. Annual Review of Microbiology 66: 285-303.

46. Hazelbauer GL, Falke JJ, Parkinson JS (2008) Bacterial chemoreceptors: high performance signaling in networked arrays. Trends in Biochemical Sciences 33: 9-19.

47. Heekeren HR, Marrett S, Ungeleider LG (2008) The neural systems that mediate human perceptual decision making. Nature Rev Neuroscience 9(6): 467-479.

48. Larsen SH, Reader RW, Kort EN, Tso WW, Adler J (1974) Change in direction of flagellar rotation is the basis of the chemotactic response. Nature 249(452): 74-77.

49. Malys N, McCarthy JEG (2011) Translation initiation: variations in the mechanism can be anticipated. Cellular and Molecular Life Sciences 68(6): 991-1003.

50. Margolski R (2002) Molecular mechanisms of taste transduction. Pure and Applied Chemistry 74(7): 1125-1133.

51. Meyer KM, Soldaat LI, Auge H, Thulke HH (2014) Adaptive and selective abortion reveals conditional decision making in plants. American Naturalist 183(3): 376-383.

52. Makagawa S, Niimura Y, Miura KI, Gojobori T (2010) Dynamic evolution of translation initiation mechanisms in prokaryotes. Proceedings of the National Academy of Sciences of the United States of America 107(14): 6382-6387.

53. Pfeffer W (1883) Directional locomotor movements by chemical stimuli. German Botanical Society Reports 1: 524-533.

54. Pfeffer W (1897) Plant Physiology, Leipzig; The Physiology of Plants, translated by AJ Ewart, 1906, Oxford at the Clarendon Press.

55. Riley M, Abe T, Arnaud MB, Berlyn MKB, Blattner FR, et al (2006) Escherichia coli Kt2 a cooperatively developed annotation snapshot - 2005. Nucleic Acids Research 34(1): 1-9.

56. Silverman M, Simon M (1974) Flagellar rotation and the mechanism of bacterial motility. Nature 249(452): 73-74.

57. Tsang N, Macnab R, Koshland DE (1973) Common mechanism for repellents and attractants in bacterial chemotaxis. Science 181(4094): 60-63.

58. Vang LL, Adler J (2016) Drosophila mutants that are motile but respond poorly to all stimuli tested. Mutants that have a large defect in interaction with stimuli or in executive function. bioRxiv p.1-37.

59. Vang LL, Adler J (2016) Drosophila mutants that are motile but respond poorly to all stimuli tested. bioRxiv p.1-12.

60. Vang LL, Adler J (2017) Drosophila mutants that are motile but respond poorly to all stimuli tested. bioRxiv p.1-12.

61. Vang LL, Adler J (2017) Drosophila mutants that are motile but respond poorly to all stimuli tested. bioRxiv p.1-14.

62. Vang LL, Adler J (2018) Drosophila mutants that are motile but respond poorly to all stimuli tested, Response by various mutants and a proposal. bioRxiv p.1-19.

63. Vang LL, Adler J (2018) Drosophila mutants that are motile but respond poorly to all stimuli tested: An intermediate called "The Boss". bioRxiv p.1-17.

64. Wohlleben P (2015) The Hidden Life of Trees. What They Feel, How They Communicate. English translation of this book, Random House GmbH, Greystone Books.

65. Zucker CL, Ebinsker B (2001) Complexities of retinal circuitry revealed by neurotransmitter receptor localization. Program in Brain Research 131: 71-81.

 How to cite this article: Julius A. Every Organism has its own "The Boss". Behavior of Bacteria Compared to Behavior of Eukaryotes. Anatomy Physiol Biochem Int J: 2023; 6(5): 555698. DOI: 10.19080/APBIJ.2023.06.555698

DOI: 10.19080/APBIJ.2023.06.555698